Bulletin of Experimental Biology and Medicine, Vol. 116, № 11, November, 1993

Decrease of Hydrodynamic Resistance in Rat Mesenteric Arterioles in Response to Injection of Polyethylene Oxide Polyox WSR-301

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UDC 532/35

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol.116, № 11, pp. 552-555, November, 1993
Original article submitted June 3, 1993

Key Words: *vascular resistance; microcirculation; polyethylene oxide*

Adequate blood supply of tissues and organs is essential to the normal functioning of the organism. From the hemodynamic point of view, this is achieved, in particular, through variation of the ratio between local microcirculatory resistances. Since the classical studies of Poiseuille [6], the role of the diameter of resistive vessels - arterioles - in the total blood flow resistance and in the redistribution of the blood flow in the microcirculatory bed has been well documented. However, the particular contribution of the flow pattern to these processes, for example, microdisturbances caused by the pulsatile flow, the movement of formed elements in a shear flow, at bifurcations of the vessels has been less studied, primarily due to methodological complications of both a physiological and a mathematical nature. High-molecular linear polymers are widely used in hydrodynamics, as they reduce the hydrodynamic resistance of the liquid by acting on the fine structure of the flow [3,9]. When injected into the circulation, these substances reduce to a greater or lesser extent the total vascular resistance due to a drop of the systemic arterial pressure and/or increase of the cardiac output [2,7]. We investigated the microcirculatory impacts of these "flow-smoothing" substances and their effect on the hemodynamic characteristics of the blood flow in arterioles.

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MATERIALS AND METHODS

Male Wistar rats weighing 200-300 g were narcotized with nembutal (50 mg/kg, intraperitoneally) and placed on a thermocontrolled stand. The rectal temperature was measured with a Model MTA-III, type 219, SE thermosensory transducer (Japan) and maintained at a constant level (36.5°C). Control animals were injected with standard physiological saline (pH 7.4) through *v. jugularis* with the aid microinjector (0.15 ml/min, 1 min). Experimental animals were injected via the same route with polyethylen oxide Polyox WSR-301 (Union Carbide, USA), dissolved in physiological saline one day before the experiment. The injection dose was 10^{-5} g/ml, and the final concentration in the blood was approximately 10^{-7} g/ml. This dose allowed for reproducing the effect several times using the same animal.

For systemic monitoring of the reactions arterial pressure (AP) on the carotid artery was measured in all animals using a Statham P-23 membrane transducer (USA). *In vivo* biomicroscopy of

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TABLE 1. Vascular Pressure (P) in Arterial Vessels (A) and Systemic AP before (Background) and after (Postinjection) Injection of Polyethylene Oxide (PO) or Physiological Saline (PS) ($M \pm m$)

Experimental conditions		n	d, μ	Background		Postinjection	
				P, mm Hg	AP, mm Hg	P, mm Hg	AP, mm Hg
radial A	PO	17	158±8	80.9±3.6	123±4	63.1±3*	105±4*
	PS	16	159±14	75.3±3.1	114±2	75.2±3.2	114±2
Arterioles	PO	21	24±1	35.2±1.1	104±2	29.3±1.2*	87±3*
	PS	9	24±1	33.3±2.4	104±1	33.4±1.8	104±1

Note. Here and in Tables 2–4: n: number of vessels; d: inner diameter; *: $p<0.01$ in comparison with control values.

the smallest radial mesenteric arterioles (lumen diameter 10.6-30.4 μ) was performed. In two experimental series: 1) native vessels and 2) adenosine-predilated vessels (10^{-5} M, irrigation of entire accessible surface) the intravascular pressure was recorded, as described elsewhere [10], using sharpened microelectrodes filled with 1.5 M NaCl (external diameter 1.5 μ), a Model 4-A, IPM standard micromanometer (USA), and an MBI-15 microscope (Leningrad). In the third experimental series the blood flow rate in the arterioles was measured under the same conditions by Doppler laser anemometry, using a twin-beam laser microscope [8], assembled from a LYUMAM-R-1 microscope, an LG-79-1 He-Ne laser, and an SCh-73 spectrum analyser. The beams (632.8 nm wavelength) were adjusted to cross within the central area of the vessel, the measuring volume being 30×12×15 μ^3. A cumulated Doppler spectrum (over 15-20 measurements) served as the output parameter. The rate value was calculated from the frequency of the spectrum maximum, i.e., the rate of the bulk of formed elements crossing the measuring volume. In these three experimental series the diameter of the vessels was assessed with an ocular-micrometer (ocular 7×, objective: 9× for radial arteries, 26× for arterioles, and 3.5× in the third series). In the fourth experimental series the diameter of arterioles before and after injection of test substances was measured more precisely by the method of splited image [1], using a 7× ocular and a 26× objective.

The above parameters were recorded during 0.5-1.5 min both prior to and immediately after injection of the test solutions. The parameters were averaged 1) over the above times separately in the background and postinjection phase, and, on this basis, 2) over all examined vessels in a given experimental or control group. The data are presented as means±SEM. The Student t test was applied.

RESULTS

Slow injection of the polymer into the circulation led to a 10-16% drop of the systemic AP in all experimental groups, while physiological saline did not affect this parameter. Hence, the injection of polyethylene oxide in the above dose was hemodynamically effective.

The blood pressure in individual radial arteries ranged from 54 to 113 mm Hg, and in arterioles from 25 to 48 mm Hg. The averaged data of 12 experimental and 8 control animals are presented in Table 1. As is seen from the table, the polymer induced a drop of intravascular pressure in radial arteries by 22.0% and in arterioles by 16.8% (AP dropped by 14.6-16.4%). In addition, the pressure was measured in arterioles with a diameter of 43±4 μ (8 vessels, 3 rats) and of 12.1±0.9 μ (15 vessels, 5 rats), i.e., in vessels of the preceding and next branching order in relation to the test arterioles. The pressure in these arterioles was found to drop from 48±3 to 36±3 mm Hg ($p<0.01$) and from 28.4±1.8 to 27.0±1.5 mm Hg (not reliably), respectively. AP dropped by 18%, the backgroung values being 115±5 and 114±3 mm Hg, respectively. Thus, in the main test arterioles (≈24 μ) we observed a decrease not only of the pressure value but also of its difference.

The averaged data on the blood flow rate under the same conditions are presented in Table 2. It varied from 137 to 2280 μ/sec in various arterioles (46 vessels, 7 experimental and 4 control animals). Injection of the polymer resulted in a

TABLE 2. Changes in Systemic AP and Blood Flow Rate (V) in Arterioles before (Background) and after (Postinjection) Injection of PO or PS ($M \pm m$)

Experimental conditions	n	d, μ	Background		Postinjection	
			V, μ/sec	AP, mm Hg	V, μ/sec	AP, mm Hg
PO	27	21±1	702±95	108±4	1079±155*	91±3*
PS	19	21±1	895±126	111±3	863±116	111±3

TABLE 3. Internal Diameter of Arterioles (*d*) and Systemic AP before (Background) and after (Postinjection) Injection of PO or PS ($M \pm m$)

Experimental conditions	*n*	Background		Postinjection	
		d, μ	AP, mm Hg	d, μ	AP, mm Hg
PO	151	17.8±0.9	122±1	17.7±0.5	105±2
PS	117	17.1±0.3	121±2	17.2±0.9	121±2

53.7% acceleration of the blood flow against the backgroung of a 15% drop of the systemic arterial pressure.

Thus, in the smallest arterioles the pressure value and its difference decreased as the blood flow accelerated in response to injection of the polymer into the circulation. Estimating the resistance of this generation of vessels to be approximately proportional to the ratio of the averaged intravascular pressure to the averaged blood flow rate in the corresponding vessels, we can say that injection of the polymer resulted in a 1.85-fold decrease of the hemodynamic resistance. To get such a decrease in accordance with the classical Poiseuille formula (the resistance of the vessel, *R*, is proportional to $1/r^4$, where *r* is the inner radius of the vessel), the arterioles would have to dilate by 16.6% (about 4 μ for an average 22.3-μ vessel), or by 22.8% (5 μ) in the case of R being proportional to $1/r^3$ [5]. We did not observe such a dilation under the ocular-micrometer; the diameter of arterioles remained practically unchanged.

We designed a special series of experiments (30 experimental and 17 control animals) for measuring the lumen of arterioles using a higher resolution method (accuracy of ±1.2%). The initial diameter of the vessels varied from 10.6 to 30.9 μ. In 3.3% (experimental animals) and 2.6% (controls) of cases the inner diameter of the examined vessels after injection of the polymer remained unchanged, being 20.8±3.6 μ and 17.1±3.0 μ in the experimental and control groups, respectively. (AP in response to injection dropped from 120±9 to 105±7 mm Hg in the experimental group, while in the controls it was 122±15 mm Hg before and 123±14 mm Hg after the injection). In 51.0% (experimental group) and 41.0% (controls) the diameter slightly decreased in response to injection of the polymer: from 18.5±0.5 to 17.3±0.5 μ in the experimental group (AP dropped from 122±2 to 104±2 mm Hg; $p<0.001$) and from 17.1±0.5 to 16.2±0.5 μ in the control group (AP remained on a constant level of 120±3 mm Hg). In 45.7% (experimental animals) and 56.4% (controls) of cases we observed a vasodilation. However, even in this case the polymer-induced vasodilation was just 6.6% in the experimental group (from 16.8±0.4 to 17.9±0.4 μ; AP was 123±2 and 106±2 mm Hg, respectively; $p<0.001$) and 5.26% in the control group (from 17.1±0.5 to 18.0±0.5 μ; AP=121±3 mm Hg). The averaged data are presented in Table 3. As is seen from the table, injection of the polymer into the circulation, while reducing AP by 13.9%, on the average does not affect the diameter of arterioles. These data confirm the assumption that vasodilation *in vivo* is not the main cause of the polymer-induced decrease of the vascular resistance.

For additional verification of this hypothesis, in an extra series of experiments (13 rats) polyethylene oxide was injected against the backgroung of adenosine-induced vasodilation. Adenosine in a concentration of 10^{-5} M increased the diameter of radial arteries from 191±10 to 217±11 μ, i.e., by 13.6% on average (7.2-49.7%, $n=33$). The diameter of arterioles increased from 21.3±0.3 to 28.4±0.6 μ, i.e., by 33.3% on average (20.0%-49.7%, $n=36$). In control experiments (6 rats) radial arteries ($n=8$) and arterioles ($n=20$) remained dilated throughout a period corresponding to the entire observation period in the main experimental group (radial arteries from 165±26 to 181±25 μ, i.e., by 9.7%, arterioles from 21.3±0.6 to 27±0.8 μ, i.e., by 28.2%). The summarized data are presented in Table 4. The intravascular pressure in the dilated arterial vessels varied just

TABLE 4. Vascular Pressure (P) in Radial Arteries and Arterioles and Systemic AP. Background: before (bkg) and after Injection of Adenosine (10^{-5} M, adn) and after Injection of PO against Background of Adenosine ($M \pm m$)

Experimental conditions	P, mm Hg			AP, mm Hg		
	background		postinjection	background		postinjection
	bkg	adn		bkg	adn	
Radial arteries	73.1±1.7	72.2±1.7	58.9±1.9*	117±1	117±1	105±2*
Arterioles	39.4±1.4	36.3±1.4	30.1±1.1*	115±3	112±1	96±2

slightly. In arterioles it dropped only 8% on average. The hemodynamic response of individual arterioles was heterogeneous, probably due to the mesenteric angioarchitectonics. The polymer lowered blood pressure in radial arteries by 19.4 and 18.4% (in comparison with the period before and after administration of adenosine, respectively); AP dropped by 10.3%; the pressure in arterioles dropped by 23.6 and 17.1%, respectively (AP by 14.3%).

As is seen from a comparison of Tables 1 and 4, there are no essential differences in the hemodynamic effect of the polymer on the native and adenosine-dilated arterioles.

The obtained results are in conformity with a previous report [4] that polymers in the circulation primarily affect the microdisturbances caused by movement of the formed elements of the blood. In other words, similarly to the case with rigid tubes [3], it is the changes in the flow pattern rather then dilation of the resistive vessels which determine both the macro- and microhemodynamic effect of the polymer. Moreover, according to the data reported here, the contribution of this purely flow pattern-dependent component in the resistance of arterioles may be considerable.

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Morphochemical Manifestations of Chronic Exposure of the Brain to Amphetamine and Their Correction by Delta-Sleep Peptide

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UDC 612.82.018:577.175.523].019.08

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol.116, № 11, pp. 555-557, November, 1993
Original article submitted April 27, 1993

Key Words: *amphetamine; rat brain neurons; structured proteins; aminopeptidase*

The present investigation was aimed at determining the specificity of the morphochemical response of some brain structures to injections of amphetamine, a known psychotropic drug, and at correcting amphetamine-induced changes with the use of delta-sleep peptide (DSP).

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MATERIALS AND METHODS

Experimental data were obtained using 4 groups of Wistar rats weighing 200-250 g.

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